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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/980,531	10/26/2001	Karl-Heinz Drexhage	ARDEN-JACOB	5858

20151 7590 09/26/2003

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EXAMINER

CEPERLEY, MARY

ART UNIT	PAPER NUMBER
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1641

DATE MAILED: 09/26/2003

8

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/980,531

Applicant(s)

DREXHAGE ET AL.

Examiner

Mary (Molly) E. Ceperley

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 20-43 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 20-43 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 2.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

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1) Although specific claims are cited in the rejections below, these rejections are also applicable to all other claims in which the noted problems/language occur.

2) The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3) The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4) Claims 20-37 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the preparation of some of the compounds of the formula I of claim 20 which contain the groups $-N(R_{11})(R_{12})$ and $=N^+(R_9)(R_{10})$ as described in claim 38, does not reasonably provide enablement for the preparation of compounds of formula I wherein either or both of $-N(R_{11})(R_{12})$ and $=N^+(R_9)(R_{10})$ are replaced by the groups $-OR_9$ and/or $=O$. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. Further, the method of preparation described in claim 38 and in the specification requires a ring closure reaction between **(a)** a compound of formula II which contains a required hydroxymethyl substituent in a *para* position relative to a $-N(R_{11})(R_{12})$ group on a phenyl ring and **(b)** a compound of formula III which contains a phenyl ring having a $-N(R_{10})(R_9)$ substituent. Note that in the working examples at least compounds JF22, JF 17, JF 30, JF 32, JF 42, JF 36, and JF 37 are prepared by methods other than that described in claim 38 indicating that not all compounds may be prepared by the method of claim 38.

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5) Claims 20-37 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the use of the compounds of formula I as labeling agents for immunoassays and nucleic acid hybridization assays when the claimed compounds are conjugated to a biomolecule, does not reasonably provide enablement for a method of use in any other context. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

6) Claims 20-43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a) A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 20, for example, recites specific definitions for the variable R₁-R₇ and the claim also recites "in particular..." which is the narrower statement of the limitation. See also the term "optionally selected from".

b) In claim 20, for the definitions of R₁-R₇, it is unclear what is meant to be included by the term "two or more substituents" and it is unclear from the claim language if these "substituents" are required to be present. See also, "one or more substituents" as a definition of the variables R₉-R₁₂.

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c) In claim 20, it is unclear what is meant by the term "one or more of the radicals R_1 - R_7 , in each case with adjacent substituents, form a ring system containing one or more multiple bonds". Is the "adjacent substituent" necessarily one of R_1 - R_7 ? How can a ring system be formed from one bond? What are the required components of the "ring system"? See also the definition of " R_8 and R_{8a} can form a ring system" and the definitions of R_9 - R_{12} .

d) In claim 20, the definition of R_8 and R_{8a} as "at least one of" implies that that there may be more than one of the groups R_8 and R_{8a} present. This is inconsistent with the structure depicted in the formula of claim 20. See also, the same "at least one of" definition for the variables R_9 - R_{12} and claim 30.

e) In claim 20, the definitions of R_8 and R_{8a} as "optionally selected from a C_1 - C_6 -alkyl group selected from at least one of ...one or more substituents" render the claim indefinite and confusing. It is not clear which variable definitions are related to which other variable definitions. For example, exactly which term does the definition "which optionally contains at least one of heteroatoms (sic) selected from oxygen, sulfur or nitrogen" modify?

f) For the R_9 - R_{12} definitions of claim 20, the term "polyether" is not a definition which is encompassed by the term "hydrocarbon group".

g) In claim 20, it is unclear whether $-N(R_{11})(R_{12})$ and $=N(R_9)(R_{10})$ can both be either $-OR^9$ (sic) or $=O$ or whether one of $-N(R_{11})(R_{12})$ and $=N(R_9)(R_{10})$ is $-OR_9$ and the other is $=O$.

h) Claims 27 and 28 are indefinite and confusing for the reason that exactly what ring systems are required and the structure of these ring systems is unclear. For example, can R_1 be bridged with R_{10} at the same time that R_2 is bridged with R_9 ? The use of the term "at least one of...and" is additionally confusing.

i) In claim 29, it is unclear what is meant by "a radical containing an aromatic ring system". Additionally, the term "aromatic ring system" does not appear to find antecedent support in claim 20.

j) For claim 31, the variable R_{12} does not appear in the formula IVE.

k) For claims 32-36 it is unclear where the "group capable of covalent coupling" is located on the structure.

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l) For claim 38, for the terminal group Y, the definition of "thio" (a non-terminal group) is inappropriate.

m) It is unclear what is meant by the claim 43 limitation "wherein the compound (I) is obtained without isolation of intermediates" and this limitation appears to be unrelated to the process of claim 38.

n) The structure of the group "4-diaminomethylphenyl" of claim 26 is unclear.

7) Claims 20-25 are rejected under 35 U.S.C. 112, second paragraph, as failing to set forth the subject matter which applicant(s) regard as their invention. Claim 20 provides for the use of specific compounds as labeling groups, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

8) Claims 20-25 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

9) Claim 37 is objected to as being a duplicate of claim 26. The "labeling agent" of claim 37 comprises the same set of "compounds" recited in claim 26.

10) The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

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(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11) The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

12) Claim 26 is rejected under 35 U.S.C. 102(b) as being anticipated by each of Hallas (reference Y of form PTO-1449), Aaron et al (X) (reference X of form PTO-1449), Aaron et al [R] (J. Chem. Soc. (1963) pp. 2655-2662), Barker et al (J. Chem. Soc. [Section B: Physical Organic] (1969), vol. 9, pp 1068-1071 or Mueller et al (U.S. 4,320,940).

a) The compound of formula (III) of Hallas wherein R = adamantyl anticipates a compound of formula I of claim 26 wherein R₄ is defined as "cyclic hydrocarbon" (see definitions of claim 20).

b) Compounds (VIII) and (IX) of Aaron et al (X) anticipate a compound of formula I of claim 26 wherein R₃ and R₄ "form a ring system containing one or more multiple bonds" (see definitions of claim 20).

c) Compounds (V) and (VI) of Aaron et al [R] wherein R = ethyl anticipate compounds of claim 26 wherein R₄ = ethyl.

d) Compound (V) of Barker et al wherein R = *p*-C₆H₄-NMe₂ anticipates a compound of formula I of claim 26 wherein R₄ is substituted phenyl (see claim 20 definitions).

e) The compound of column 6, line 35 of Mueller et al anticipates a compound of claim 26 wherein R₂ and R₃ "form a ring system containing one or more multiple bonds" (see the definitions of claim 20).

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13) Claims 29 and 30 are rejected under 35 U.S.C. 102(b) as being anticipated by each of Aaron et al [R] and Mueller et al (U.S. 4,320,940).

Compounds (V) and (VI) of Aaron et al [R] wherein R = ethyl anticipate compounds of claims 29 and 30 wherein R₄ = ethyl.

The compound of column 6, line 35 of Mueller et al anticipates a compound of claims 29 and 30 wherein R₂ and R₃ "form a ring system containing one or more multiple bonds", R₄ = H, and R₈, R_{8a} = methyl (see the definitions of claim 20).

14) Claims 26, 29 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over each of Hallas (reference Y of form PTO-1449), Aaron et al (X) (reference X of form PTO-1449), Aaron et al [R] (J. Chem. Soc. (1963) pp. 2655-2662), Barker et al (J. Chem. Soc. [Section B: Physical Organic] (1969), vol. 9, pp 1068-1071), or Mueller et al (U.S. 4,320,940).

The cited references are applied for their description of compounds as set forth in paragraph **12) a) – e)** above. See also, Aaron et al [R], Table I; Hallas et al, compounds wherein R = H, t-Bu; Barker et al, Table of page 1069. Although certain structures of the formula I of claim 26 are excluded by provisos, the remaining structures of formula I of claim 26 which are not excluded by these provisos include compounds which are obvious over the closely structurally related compounds of the prior art in accordance with the decisions in In re Wood, 199 USPQ 137; In re Payne et al, 203 USPQ 245; and In re Grunwell et al, 203 USPQ 1055. For example, the structure (III) of Hallas et al wherein R = t-Bu renders obvious the corresponding compound of claim 26 wherein R₄ is Et or Pr, R₉-R₁₂ = Me and the Hallas et al compound (III) wherein R = t-Bu renders obvious the compound of claim 26 wherein R₉-R₁₁ = Me and R₁₂ = Et; the compounds (V) of Barker et al wherein R = OH or Ph render obvious the compounds of claim 26 wherein R₄ = OH or Ph and R₉-R₁₁ = Me and R₁₂ = Et. There is an expectation that closely related structures would have the same or similar utility; both the claimed compounds and the compounds of the prior art have utility as organic dyes.

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15) Claims 20-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over each of **a)** Hallas (reference Y of form PTO-1449), Aaron et al (X) (reference X of form PTO-1449), Aaron et al [R] (J. Chem. Soc. (1963) pp. 2655-2662), Barker et al (J. Chem. Soc. [Section B: Physical Organic] (1969), vol. 9, pp 1068-1071), or Mueller et al (U.S. 4,320,940) taken in combination with each of **b)** Dorval et al (U.S. 5,561,045) or Bandman et al (U.S. 6,183,968).

Each of references **a)** is applied for the reasons set forth in paragraphs **12)** through **15)** above.

Dorval et al and Bandman et al are applied for their teaching that fluorescent dyes of the type claimed herein and of the type described in references **a)** are useful as labels in immunoassays and nucleic acid hybridization assays. See Dorval et al, col. 6, line 48 – col. 7, line 60; col. 8, lines 49 – 65; in particular col. 7, line 22; Bandman et al, col. 8, line 63 – col. 9, line 16, in particular, col. 9, line 8.

In view of the fact that the compounds of the instant claims and closely related compounds (references **a)**) are known to be fluorescent dyes, it would be obvious to substitute the fluorescent dyes of references **a)** as equivalent fluorescent labels in the immunoassays and nucleic acid hybridization assays of references **b)**, as claimed, with the expectation of obtaining similarly useful assays based on a fluorescence detection method.

16) Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary (Molly) E. Ceperley whose telephone number is (703) 308-4239. The examiner can normally be reached from 8 a.m. to 4:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le, can be reached on (703) 305-3399. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556 or (703) 305-3592.

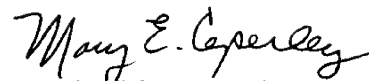
Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

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September 23, 2003

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A handwritten signature in cursive script, reading "Mary E. Ceperley".

Mary (Molly) E. Ceperley
Primary Examiner
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